REMARKS

Applicants note with appreciation the Examiner's withdrawal of the objection to the Specification. Applicants further note with appreciation the Examiner's withdrawal of the prior claim objections under 37 C.F.R. §1.75(c). Further, the Applicants note with appreciation the Examiner's withdrawal of rejections under § 112, first and second paragraphs, as well as the withdrawal from rejections under 35 U.S.C. §§§ 101, 102 and 103.

Turning now to the maintained rejection under 35 U.S.C. § 112, second paragraph, the Applicants submit that as a result of the amendment to Claim 7 changing "DHCP" to "4,5-dihydroxy-2-cyclopenten-1-one" the rejection of Claim 7 under 35 U.S.C. § 112, second paragraph is now obviated. Further, in regards to the Examiner's rejection under 37 C.F.R. §1.75(c), the Applicants have amended Claim 8 in accordance with the Examiner's helpful suggestion to change the phrase "from *E. coli*" to "native to *E. coli*", thus, further defining the subject matter.

Claims 7 and 8 are rejected under 35 U.S.C. §§ 102(b) and 103 as being anticipated by or obvious over Blattner et al. Applicants respectfully submit that the identification and characterization of open reading-frame 389 (*dep*) as responsible for resistance to DHCP in a multi-copy plasmid is not anticipated by the identification of the genome sequence of *E. coli* K-12 as described in Blattner et al. Applicants respectfully submit that until the Applicants' discovery there had been no characterization or identification of a gene that was responsible for conferring resistance to DHCP. Prior to the Applicants' discovery Blattner et al. provided a broad generalized structure of the *E. coli* genome. The rejection asserts that because Blattner et al. has provided the *E. coli* genome, it has **inherently** described the function of the Applicants' claims. Applicants invite the Examiner's attention to the following passage from Blattner et al., which states that:

> Currently, the annotation includes 4,288 actual and proposed protein coding genes, and one-third of these genes are well characterized. Postulation of genes and uncharacterized base sequences was surprisingly difficult....Pending the location of the coding sequences for 383 known *E. coli* proteins that are not yet associated with ORFs, **nearly 40% of the ORFs are completely uncharacterized.** (Blattner et al, pg. 1454, left column, lines 21-26; pg. 1454, line 60 to 1459, line 1).

Applicants respectfully submit that open reading-frame 389, which the Applicants have named *dep,* was one of the myriad of uncharacterized open reading-frames cited by Blattner et al. As a result, Applicants respectfully submit that Blattner et al. fails to characterize a gene which is capable of acting as a DHCP efflux protein.

Applicants respectfully submit that Blattner et al. fails to teach the isolation and characterization of the particular locale, namely, ORF389 that transports a DHCP efflux protein. Blattner et al. provided no identification as to where the *dep* starts or where it ends, and hence failed to show the isolation of *dep* from *E. coli.* In view of this fact and in further view of the uncharacterized open reading-frames of the *E. coli* genomes described in Blattner et al., one skilled in the art would be completely unaware of where the *dep* coding gene was located on the *E. coli* genome.

The Examiner is asked to consider the case of *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 13USPQ2d (D. Mass. 1989), Judgement aff-d in Part, Vacated in Part on Other Grounds, 13 USPQ2d 1014-1016 (Fed. Cir. 1991). In *Amgen*, the Federal Circuit noted that the "obvious to try" standard did not offer a reasonable expectation of success for the Applicants. In drawing this conclusion, the Federal Circuit stated that simply because the overall homology of the baboon DNA and human DNA was approximately 90%, it was only "obvious to try" using a monkey probe.

Amgen, Inc. 13 USPQ2d 1018. Consequently, using a monkey probe would not have been obvious. **The Court went on to further note that there are many pitfalls in probing and isolating sequences. Id.**

Applicants respectfully submit that 35 U.S.C. § 102 requires that the invention, including each element and limitation of the claims, was known or used by others before it was invented by the patentee. *Hoover Groups Inc. v Custom Metalcraft, Inc.* 36 USPQ2d 1101, 1103 (Fed. Cir. 1995). In view of this precedence, Applicants respectfully submit that the Applicants' claimed limitation to a DHCP efflux protein (*dep*) is neither expressly nor inherently described in Blattner et al. Specifically, Blattner et al. must describe and enable the claimed invention including all the claimed limitations, with sufficient clarity and detail to establish that the subject matter already existed in the prior art and that it's existence was recognized by persons of ordinary skill in the field of the invention. *Crown Operations International, Ltd. v. Solutia, Inc.*, 62 USPQ2d 1917, 1921 (Fed. Cir. 2002). Nowhere in Blattner et al. is there a disclosure as to the identification and characterization of a DHCP efflux protein. Nowhere within the four corners of Blattner et al. is there a description of isolating, purifying and characterizing a DHCP efflux protein. In fact, prior to the Applicants' invention the art was unaware whether the *E. coli* genome contained a gene that conferred resistance to DHCP. Consequently, the Applicants had to develop a protocol to screen the *E. coli* genome library for genes that conferred resistance to DHCP. (Applicants' specification page 11, lines 12 to page 12, line 8). In view of the foregoing, the Examiner is asked to consider the oft-sighted passage from the words of Judge Hand:

> No doctrine of the patent law is better established in that a prior patent or other publication to be an anticipation must bear within its four corners adequate directions for the practice of the patent invalidated. If an earlier disclosure offers no more than a starting

> point for further experience, if it's teachings will sometimes exceed and sometimes fail, if it did form the art without more how to practice the new invention, it is not correspondingly enriched the store of common knowledge, and it is not anticipation.

With this background in mind, it is respectfully submitted that nowhere in Blattner et al. is there a teaching that the *E. coli* genome as identified by Blattner et al. discloses an isolated gene that confers resistance to DHCP. Nor does Blattner et al. identify a method to screen a *E. coli* genome to test for a gene that would confer resistance to the DHCP.

Applicants respectfully submit that an inherent limitation is one that is necessarily recognized by those skilled in the art and that invalidation based on inherency can not be established by probabilities or possibilities. *Scaltech, Inc. v. Retec/Tetra, LLC.* 51 USPQ2d 1055-1059 (Fed. Cir. 1999). Applicants respectfully submit that the identification of a gene capable of transporting DHCP out of a bacterial cell was not known to exist at the time of the Blattner et al. reference. In fact, until the characterization and identification by the Applicants, the art was unaware that a *dep* gene was present in *E. coli*. Thus, the existence of a *dep* gene in the genome of *E. coli* was not recognized by persons of ordinary skill in the field of the invention.

Courts have recognized that anticipation is avoided when a product is produced repeatedly as a minor and unrecognized contaminant. *In re Coordinated Pre-trial Proceedings in Antibiotics Antitrust Actions,* 210 USPQ 673 (EDPA. 1980), Judgment AFF'D 216 USPQ 1056 (3d Cir. 1982). This case held that "co-production of small amounts of tetracycline in the prior art, which was unrecognized at the time of the Conova invention, could not act as a bar to the patent on tetracycline." Id. Similarly, although Blattner et al. may have described in general terms the entire *E. coli* genome, it did not recognize the small *dep* gene, which encoded for the DHCP efflux protein.

Specifically, Blattner et al. annotated 4,288 protein-coding genes, 38% of which had no attributed function. Of these 4,288 annotated genes, the Applicants have isolated and identified one gene, which encoded for a DHCP efflux protein. In view of the above-mentioned case, the Applicants respectfully submit that the *dep* gene was at best merely a minor unrecognized contaminant of the *E. coli* genome.

Claim Rejections Under 35 U.S.C. § 103

Claims 10 and 12 have been rejected under 35 U.S.C.§ 103(a) as being unpatentable over Blattner et al. over Weickert et al. The rejection asserts that Blattner et al. describes a putative transport membrane protein *ydhC*. Applicants, however, have thoroughly searched the reference, and find no mention of *ydhC*, which the Applicants have defined in the specification and respectfully submit is well known in the art as encoding a homologue of bicyclomycin resistance protein. (Berlyn et al., 1996). As a result it is respectfully submitted that *ydhC* is not a putative transport membrane protein.

Applicants respectfully submit that the mere fact that the prior art could be so modified does not make modification obvious unless the prior art suggests the desirability of modification. *In re Gordon et al.* 221 USPQ 1125 (Fed. Cir. 1984). Applicants respectfully submit that nothing in Blattner et al. suggests the desirability to express the *dep* gene in a multi-copy plasmid. Because Blattner et al. failed to characterize *dep* as a DHCP efflux protein, one skilled in the art lacked any motivation or suggestion to make and analyze the biochemical and catalytic activity of the *dep* protein. Hence, one skilled in the art had no motivation to over produce a gene which lacked any associated function. Furthermore, Applicants respectfully submit that the passage cited in the current

Office Action which states that Blattner et al. specifically suggests that "an analysis of biochemical and catalytic properties of the expressed proteins", merely offers a general invitation "to try". Specifically, the beginning of the aforementioned passage in Blattner et al. states that:

> this represents only the beginning of all understanding. Further research will be required to determine the precise functions for all the genes.

Blattner et al. has not described a gene coding for a DHCP efflux protein and consequently, one skilled in the art has no motivation to over produce a protein which in Blattner et al. is completely uncharacterized. Furthermore, it is respectfully submitted that one skilled in the art would have no motivation to over produced an uncharacterized protein, as the skilled artisan would be left fishing in the dark without the proper assay design to understand the role of the "over produced" protein.

In view of the foregoing, Applicants respectfully submit that the amended claims are now in condition for allowance, which action is respectfully requested.

Respectfully submitted,

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